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THE PRESENT ASPECT

OF THE CANCER PROBLEM

BY

ROSWELL PARK, A.M., M.D.

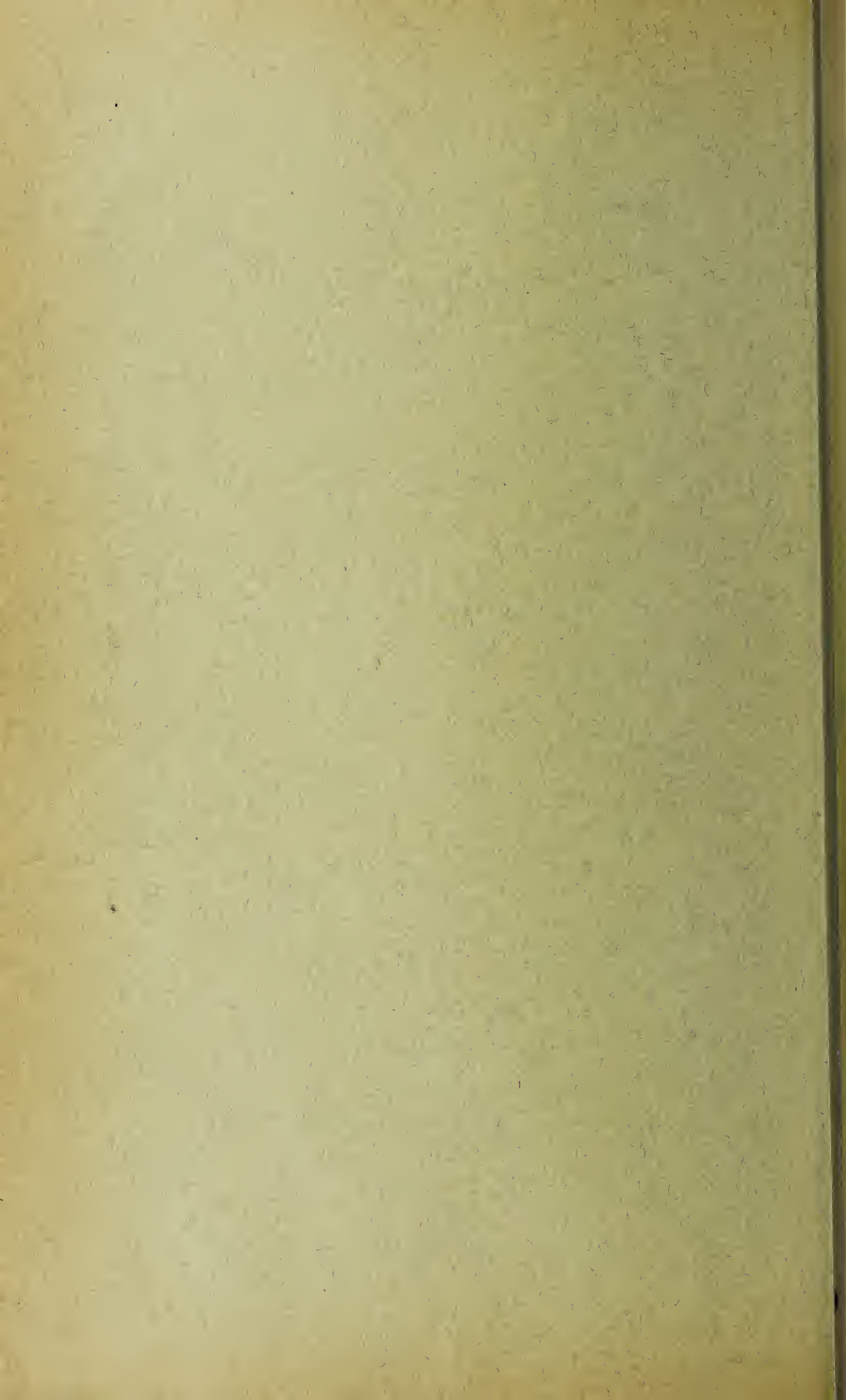
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THE PRESENT ASPECT OF THE CANCER PROBLEM.

BY ROSWELL PARK, A.M., M.D.,

Professor of Surgery Medical Department University of Buffalo.

The most important problem in pathology of to-day is still the cancer problem. It is likewise the most inscrutable. It continues to engage, as must, the attention of all students of pathology and research workers, and never was it attacked from so many different directions as at present. Although, so far as final solution is concerned, it still remains theiddle of the ages, nevertheless a great deal of light has been thrown upon its perplexities by research of the past few years. In this systematic investigation New York State has been the pioneer, and the Cancer Laboratory, now working as a department of the New York State Department of Health is, as it has been since its organization five years ago, an exceedingly active center for such investigation. The studies which have proceeded from this laboratory have engaged the attention of the most earnest thinkers the world over, and have given prominence to the effort here making to solve at least some of the moot questions concerning this dread disease.

Five years ago, when endeavoring to secure state aid for this purpose, I called attention in a variety of ways and in different publications to the ready increase in the disease, taking

for the purpose at that time the population of New York State, and showing what a rapid increase in mortality could be noted, decade by decade, in the State Board of Health returns. Incidentally the position was taken that this increase concerned not New York State alone, but a large part, at least, of the civilized world. These statements had a force which was almost dramatic and were challenged in various places and by various writers. They stand to-day practically unchanged after all the assaults made upon them, and more than this, confirmed by statisticians at home and abroad, who have not been able to explain away the figures presented by any theory save that including the actual fact. Maps and figures have been published in Great Britain, in Germany, and in many States of this country, which fully corroborate the general statements that I made some years ago. The force of the argument is not lost, even supposing that the critics are in some measure correct in the statement that the increase is to be explained largely on the ground of improved diagnosis. For if this be so, while the rate may not be increasing quite so rapidly, nevertheless it shows what a number of deaths are actually occurring from

this disease, and stamps it as equally important and equally deserving the attention of the highest sanitary and public authorities. In this connection, and without wearying you with figures, I would simply like to call your attention to some figures gathered by a perfectly unprejudiced student of the subject, Dr. F. F. Simpson, of Pittsburgh, Pa. Early in 1901 he addressed notes to the Boards of Health of many of the larger States of this country requesting facts regarding population, the total number of deaths, and the number attributed to cancer for each year from 1890 to 1899. From these official reports it would appear that for 1899, twenty-two States with an aggregate population of 9,359,600 reported their total deaths to be 169,608, while their deaths ascribed to cancer aggregated 5,486. It therefore would appear that of all deaths in those States for that year, one in every thirty-one was due to cancer. If we accept the view that almost all deaths from cancer occur in those over thirty, and accept at the same time the data upon which life insurance companies base their risks, viz.: That 56 per cent. of deaths occur under the age of thirty, we are safe in the conclusion that of all who die over the age of thirty, one in fourteen dies of cancer.

Out of a number of tables which he prepared, there is one showing the relative number of deaths from cancer and from all causes in the years given, most of this information coming from the U. S. Census reports.

1850—1	death from cancer to	156	deaths from all causes		
1860—1	"	"	109	"	"
1870—1	"	"	79	"	"
1890—1	"	"	47	"	"
1900—1	"	"	35	"	"

From this it will appear that within the past fifty years the proportion of deaths from cancer has risen from one in 156 to one in thirty-five, or, in round numbers is five times greater than in 1850. These figures are startling, and, moreover, have the corroboration of independent observers in several different parts of the world.

But statistics make poor reading to the public, and I am quite willing to substantiate all that I have claimed in this direction.

With regard now to the nature of the disease, the problem may be summed up, I think, in these words: Cancer is cell anarchy or cell rebellion, if you will, provoked by some agency. When we know the exact nature of this excitant, we shall have the basis for our work. It must come, however, either from within the cell or from without. What it is that makes cells act in the way in which they do in this disease, is the great question. The evolutionists and the biologists have been trying to solve this problem, either on broad general considerations, or by examining cells through the microscope, and both have missed the very important clinical question which we cannot afford to miss. We are to square ourselves with the facts. Absolutely no explanation is afforded for this peculiar cell activity which can come from within the cell alone. Neither atavistic tendencies, hereditary influences nor any other explanation which can be framed in advance suffices for this purpose. The explanation and can be but one explanation: some extrinsic influence brought to bear upon the cells alone suffices.



EXPERIMENTAL TRANSMISSION OF SARCOMA (INTRAPERITONEAL) FROM RAT TO RAT. L. LOEB.

explain their morbid activity. Summed up in its comprehensive significance this means the parasitic theory of cancer, which has not yet been reduced to a question of what parasite, but rests at present upon the broad and indefinite plane of mere parasitism. Histologists and the old line pathologists who adhere to conventional views will never decide this matter. It must be viewed from a wider standpoint than that afforded by the brass tube and the lens at either end of it. I cannot help repeating here the fact to which I have more than once publicly alluded, that there is no other disease characterized by metastasis in which the pathologist declines to see a parasitic, *i. e.*, an infecting and infectious agent. Why is it then that he refuses so blindly to see it in this particular instance? There is no other disease even characterized by progressive infiltration which has not a parasitic cause or a parasite as a cause. I should keep repeating my own arguments were I to rehearse here all that might be said in favor of the parasitic hypothesis, of which I have been for years a most ardent advocate. To very positive arguments which might be adduced in its favor, are opposed mere negations by those who cannot accept it.

But the strongest arguments which can be adduced in favor of it must be those which experimentation or accurate clinical observation may afford. In this direction I would call your attention to the experimental results already reported from the Buffalo Laboratory by Dr. Gaylord, and especially to the photographs which I pass around showing the experimental

results of Dr. Leo Loeb, who worked especially with small animals and particularly rats. It has appeared more and more to the experimenters in this direction that cancer can hardly be transmitted from animals of one species to those of another but that it can be experimentally transmitted from one animal to another of the same species. Dr. Loeb has brilliantly demonstrated in the photograph exhibited here is one of his experimental animals, one of a large series in which he transmitted the disease by intra-peritoneal inoculation. The original tumor appeared as a sarcoma in an animal secured by him, and he has already succeeded in producing the disease in from 200 to 300 animals of the same species. This particular specimen shows an intra-abdominal growth thus produced within a few weeks, photographs being made by Dr. Gaylord. (Dr. Loeb's paper, *Journal of Experimental Medicine*, 1901). Such an unbroken series as this would seem to quite do away with all the objections of the old line pathologists as to failure in transmission of the disease from animal to animal.

Contrast with this, again, the photographs which I show you of the heart and liver from a patient whose history, briefly, was as follows: This patient was twenty-four years of age and for a long time and up to his death, under the observation of Dr. G. W. Wende of Buffalo, with whom I repeatedly saw him. There is no family history of any cancerous lesion. He had a congenital pigmented mole on the shoulder, and in his occupation was compelled to carry heavy firkins of lard, which he usually re-

on this shoulder, and by which he constantly irritated this little con- genital growth. He was noted for strength, and it was said of him that he could lift a horse. By this friction he produced at this point an sore which would not heal. At a homœopathic hospital a ligature was around this growth so that it fell but it soon returned with a cluster growths around it, some of which were pigmented and some not. One of the photographs shows the appearance of the back shortly after this condition was noted. (Fig. 2.) When seen by Dr. Wende he had between 200 and 400 pigmented and unpigmented small tumors of the scattered all over the body. When seen by me he was suffering from anæmia, and all the clinical evidences of mediastinal growth, and all with every clinical evidence of extensive metastatic involvement of the viscera. The *post-mortem* made by Dr. Wende and Gaylord showed this to be the case, and the heart and liver were in a condition indicated by the illustrations. Under the microscope the picture was of rapidly growing carcinoma. (Figs. 3 and 4.)

Who can now view such a case as that and fail to compare it with the most extensive and rapid spread of, for instance, tubercular disease? And who can say, viewing either the slides or the gross specimens that this sort of condition can be brought about by anything but an infectious agent? Evidence of an entirely different character is afforded by the study of the so-called "cancer houses" and of cases occurring endemically, or in family groups. One of the best of recent studies of "cancer a deux," as the

French call it, is that by Behla, who has already done so much in this line of investigation. (*Deutsch. Med. Wochschr.*, 1901, No. 26). He has here brought together a surprising number of cases of this kind, and of instances which stamp the disease as almost more than infectious, it appearing to be even in some instances actually contagious. From such sources and many others we can get ample justification for the statement made by Czerny that there is more reason for believing in the infectiousness of cancer than of leprosy. Additional argument against heredity of the disease can also be furnished by this statement that there is, so far as is known, not a single case on record of cancer in the new-born, and that it develops in human beings at a time when they are farthest removed from any hereditary influences.

Passing now from these aspects of the problem, let us consider some of its bio-chemical phases. Cellular morphology is far from being an exact science. There are minute differences between tumors which appear almost identical, and there are marked resemblances in tumors which appear very different from one another. No matter what the microscope may reveal, the clinician is quite able to affirm that most varying and variable conditions are obtained in different tumors. There is as much difference between cells of the same type and between their appearances as there is in shape between human noses. For instance, one case of epithelioma will proceed so exceedingly slowly as to become an affair of years' duration, while, at other times, its course may be so rapid as to stamp it as possessing the highest degree of malignancy. These

changes are not to be explained by the shape of cells nor character of surrounding tissue; they still constitute a part of the mystery of cancer.

Nevertheless, something of light has been shed upon these differences in cell growth by bio-chemical investigations, such as those made, for instance, by Brault (*Le Prognostic des Tumeurs base sur Glycogene*, Paris, 1899), which pertain to the amount of glycogen present in the tissues of certain tumors. In various papers he has shown the prognostic value attaching to such researches. All tumors, without exception, contain a certain proportion of glycogen, especially those of epithelial origin. This glycogen seems to be stored up as a sort of reservoir of potential energy, whose quantity is a measure of the possibility of rapid cell action.

It is a rather curious fact that while histology demonstrates certain fundamental differences between sarcoma and carcinoma, for instance, these differences are not maintained or cleared up by chemical activity of the cells which constitute the tumors. For instance, in sarcoma of a limb there may be present an enormous accumulation of glycogen, and this whether the cells assume the small, round, or the large spindle shape. Even in benign tumors glycogen is not lacking, for it has been observed in almost every one of them. This is important, for it would seem to show that glycogen is an index—not of malignancy, but of rapidity of growth, *i. e.*, as said above, of potential energy. The glycogenesis noted in tumor formation is not distinguished by any important peculiarity, for it proceeds normally in various parts of the body, as, for in-

stance, the liver and the muscle. Tumors, like other parts of the body are simply collections of cells, whose growth does not seem to follow such fixed laws, however, and which seem to have escaped from certain impulses. In sarcoma, for instance, the cells, though pushed to a certain distance from centers and deprived more or less of normal secretions, preserve nevertheless the faculty of storing glycogen, no matter what their shape or size. Whether these tumors develop in the liver or at a distance there seems no difference in their glycogenic contents, nor does it matter whether, when in the liver, biliary passages are closed or not. In fact, glycogenesis is simply a cell function and it is not the exclusive property of any particular organ, but is necessarily inseparable from the activity of all minor growths and cannot be localized. It is also worthy of note that the glycogen thus formed does not act, though it were a secretion to be formed and used for a purpose, but is simply stored up, as it were, in a reservoir for use when needed. A careful chemical study, therefore, of tumors will show that the glycogenic efficiency of their tissues are indicative to the degree of their malignancy, and to the possibility of their rapid formation.

The relations between inflammation and cancer formation seriously concerned the minds of the pathologists of the earlier part of this century than that preceding. For instance, Brissot, who described an inflammation of the rectum, which must have been malignant, died himself of the same trouble; and writers like James in 1766, Nisbet in 1795, Burns in 1800, and



ACUTE MILIARY CARCINOSIS. REGION OF PRIMARY INVOLVEMENT; BACK. DR. G. W. WENDE.

Wenzel in 1815, ascribed all tumor growths to an inflammatory origin; which was not strange under the conditions of knowledge obtaining at that time. Even comparatively recent writers have not been lacking who ascribe the lowering of tissue resistance to an increasing blood pressure, for instance, such as is seen in the ordinary chronic inflammatory disturbances.

The subtle influence which guides epithelial formation in a pretty uniform direction has been likened to that which makes crystals of the same substance assume invariable peculiarities. They form in obedience to some unknown influence, while epithelial cells form a cancer in obedience to some mysterious law with which we are not acquainted. Nevertheless, it is undeniable that the more cells a tumor contains within a given space, the more malignant are its clinical characteristics. Ackermann (*Hellin, Struma sarcomatosa*, München, 1893), for instance, has stated that sarcoma differs from fibroma merely in this respect—that the cells have not had time to complete their progressive metamorphosis into ordinary connective tissue. Certain it is that many normal tissues are built up from small beginnings, just as are the tumors; the thyroid, for instance, as Gegenbaur has reminded us, which grows like a neoplasm. It is a growth which differentiates itself from embryonal tissue in the most significant way, and I have seen at least one case, myself, in which it seems to have continued to develop into a mass which became a tumor, and determined the death of the child. In fact, the various metamorphoses of embryonal tissue almost defy scrutiny and classification. The cells of a

lipoma, for instance, undergo a certain change which reminds one of embryonal tissue before they enter into the composition of a distinct tumor. Myxoma is almost an intermediate stage between lipoma and sarcoma and can often follow the changes as follows the tissues from benign to malignant alterations. In fact, according to Virchow, it is in one sense the incompleteness of a given tissue which furnishes excuse for development of tumor in the same. This is, perhaps, especially true of nævi. The more complicated the structure of the original tissue the greater the danger of tumor formation. The simplicity of muscle cells and of true nerve cells constitutes their exemption from tumor formation, since we have no tumor forms of striped muscle, nor of nerve cells. Not very different is the case of carcinoma of organs or parts undergoing retrogressive metamorphosis.

Many of these changes remind one also of changes that go on normally in the young tissues; carcinoma formation of the skin glands, for instance, is almost the same process as that which the epithelium grows downward and first forms them. Epithelial cells penetrate as a solid column, which undergoes a certain liquefaction that corresponds to the softening going on in many cancers. Cancer cells seem in some cases, "born" too early, and in some cases, too late. The occurrence of truly embryonal cells in adult tissue is physiologically an anachronism which some medical philosophers have been pleased to record as a sort of atavism. That which in normal tissues is transitory, in cancer remains stationary. Carcinomatous tissue is heterologous only in the develop-

mental sense, not when the embryo is considered. Cancer cells resemble the emerald insects which appear, pair themselves, reproduce their kind, and fall in the same day. There is much in the nature of cancer cells to put us continuously in mind of some atavistic process. The cells lose their function and develop wildly. Nor should we forget these peculiarities which evince themselves when cells intended for one purpose assume another function. Thus, for instance, in complete prolapse of the uterus, where the mucosa closely resembles the skin, we may find that a naturally concealed and deep lying tissue has appropriated the peculiarities of the superficial tissue. This is the most indifferent tissues which remove the most common points from which a new growth takes its origin as in cancer of the eye, for instance, since from the peculiarly specialized parts of the globe cancer rarely arises.

Hellin sums up his views on cancer treatment with this rather significant statement; the therapy of cancer must practically be an effort to prolong the duration of life of cells. To lower their temperature, to shut off their fluid supplies, would seem, according to him, to be primary indications.

In an interesting biological study regarding cancer, Hellin (*Das Carcinom; eine biologische Skizze*, Leipzig, 1898), starts out with this general statement which, of course, will find general acceptance, that between the duration of life and fecundity of a given animal or vegetable organism there is always a quite constant relation. This axiom obtains not merely for different species of animals, but also even for individual cells of both kingdoms. He makes it appear, moreover, that the natural

lifetime of a cancer cell is brief; hence, its extra activity, its tendency to rapid cell division, all of which are in obedience to this law. The more cells a cancer contains the more malignant it is, while it is universally accepted that the most malignant cancers are those which have the smallest cells, and that an increase in size of component cells gives less rapidity of cell division and diminished malignancy. This short but strenuous life of cancer cells would seem to be determined by external or internal irritation—irritation, that is, in the sense of some extrinsic influence which affects its activity. Such influences, for instance, are the heat which hatches an egg, the warmth and moisture which effect the germination of seed, etc. When such external agency acts continuously, then we may speak of its effect as a chronic irritation and expect constant results. Among such irritations trauma has always been regarded as constituting perhaps the most important, or at least the most demonstrable, but mechanical injury is only one phase of the general subject of irritation from without, which should be made also to include temperature changes, the influences of chemical activity, etc. Cancer of the stomach, for instance, which is perhaps the most frequent of all varieties, occurs where irritation is most constant and if we seek for those other parts of the body where cancer is most constant we find them about the uterus, the breast, the rectum and intestines and the face. In other words, in those positions which are most exposed to direct infection, or other irritation. We see the influence of dirt upon the skin, for instance, in cancer of the face in the lower classes, in cancer of the lip,

in paraffine cancer, chimney sweepers' cancer, etc. These points of predilection are not merely those exceedingly exposed, but are those also where regeneration occurs least kindly, *i. e.*, at points where the skin and mucous membrane meet, because along these lines there is a variation in the type of cell structure. The only apparent exception is, perhaps, in the liver, which is still known to be an organ exceedingly capable of regeneration, and which is rarely the seat of primary cancer. This is due, probably, not so much to its functional peculiarities as to its protected position, and yet, even here we know what the irritation of gallstones may produce.

We have not yet learned what the mysterious influence is which, in most cases, controls the size and shape of a growing mass and converts it into an organ or a part of one type or another. We may call it polarity, or call it what we will. At all events, we cannot refuse to recognize it. In cancerous growths it would seem as if this particular influence were lacking or had not made itself completely felt, because in cancer there seems to be absolutely no regulation of the process of cell growth which proceeds widely and without purpose, following only the mechanical law of growth in the direction of least resistance.

It is interesting that observers like Hellin, who find little to commend in the parasitic theory of cancer, nevertheless cannot explain the rapid cell growth of tumor formations without invoking the hypothesis of some mysterious irritation. The Germans, for instance, are always talking about "chronischer Reiz," and, at the same time, explaining nothing of the state-

ments and demonstrations of other with regard to the decided parasitic nature of this *Reiz*. It is an easy thing to state with a certain pompousness of expression that increase of cells in cancer is due to their relatively strenuous and shortened lives, which is to be accounted for by the persistence of chronic or intermittent irritation. This explains nothing and should not be accepted as of much value. It is a statement, however, which probably no one will challenge, but it leads us to seek further for the nature of this alleged irritation; for which no adequate explanation has been offered, as coming from the cells themselves, and which can only be conceived of as an element intruded from without. The cell growth cannot go on indefinitely and eternally, and so comes necessarily to an end, which is the breaking down of the cancer itself. The more active the growth, the quicker its end is attained. Even crystals by the rapid or slow deposition of the molecules which form them do not grow forever, and there comes an end to the formation of every crystal, no matter how favorable the surroundings for crystalline formation. Cell division is in some respects an expression of a struggle for existence which is determined by a lack of sufficient nutrition. When nutrition is plentiful, cells attain larger size and labor less strenuously. When nutrition fails, individual enterprise must be increased. At least, this seems to be the law of cell growth. This has been helped to a certain extent by favorable temperature conditions. Increased cell activity leads to increase of heat, and each influence seems to act upon the other. A third favorable condition is access of water, which seems



FIG. 3. ACUTE MILIARY CARCINOSIS; HEART. DR. WENDE.

be an absolute necessity to animal and vegetable life. The embryo, for instance, is made up of about 87 per cent. of water, whereas adult tissues contain about 70 per cent. The same variations are seen between young and old plants. They obtain, moreover, between different portions of the same organism. In the growing tree the most rapid alterations are seen in those parts which are most moist, whereas in the thick and almost dried substance of the woody fiber, changes are much less rapid. It would seem as if the malignancy of a tumor could almost be made out by its juiciness. Certain it is that the most rapid growths are the softest and most succulent. This fact seems to have been made quite clear by Kahane (*Centralblt. für path. Anat.*, 1895, p. 673), and Beneke has emphasized how often individuals loaded with œdematous fat tissue succumb to cancer.

The reciprocal relations of cancer and tuberculosis have been the subject of very lively discussion for the past twenty years, one side holding with Hunter and Rokitansky to an actual antagonism between the two diseases, the other with Lebert, Weber and others that their coexistence amounts almost, in some instances, to a symbiosis. It was in 1879 that Picot (*Gaz. Hebdom.*, 1879) published a most complete report of a case of cancer of the liver, in which there existed, at the same time, large tubercular cavities in both lungs. This was, to be sure, before the acceptance of Koch's views and his description of the bacilli of tuberculosis. The coexistence of the two diseases is an actual fact, while those lesions which most interest the surgeon abound in regions where mucous mem-

brane and skin come together, but it is especially those particular lesions where both diseases appear in close proximity, or involve the same area, that most interest us. To be sure, this is almost equally true of syphilis and cancer, for the development of epithelioma upon a syphilitic basis is almost as common as upon a tubercular. Cruveilhier reported, in his time, to the Anatomical Society a case of so-called areolar sarcocele, which he described as both cancerous and tuberculous. It will be worth while to take a little time and with Claude (*Cancer et Tuberculose*, Paris, 1900) discuss these relations, first, the development of cancer upon a tuberculosis basis, and second, the development of tuberculosis upon a cancerous basis.

It has been a well-known fact for some time that lupus is frequently followed by epithelioma. This was, perhaps, first insisted upon by Devergie in 1854. When this transformation occurs, the disease rapidly spreads, the neighboring lymphatics become involved, and the lesion itself becomes much more painful than previously was the case. The most careful recent study of this morbid condition has been made by Desbonnets (*Epithelioma Lupus. These de Paris*, 1894). When this transformation occurs it may take place over a portion of an old lupus area which has become cicatrized, or upon the fresh active portion of its surface. Twenty-one times out of nine Desbonnets saw a cancer appear upon a cicatrized lupus area. The subject has been studied in Germany, especially by Busch, who described, in 1872, what is now generally known as lupus carcinoma. According to Busch this affection is particularly common upon

the extremities, and is often coexistent with other tubercular lesions. The particular cases of lupus most likely to undergo this change appear in the form of papillomatous ulceration which becomes cracked and fissured easily, but which yield readily to treatment by the sharp spoon. This has been called by Schütz papillomatous lupus.

In 1890 Garre published one of the first cases of lupus of the larynx undergoing cancerous degeneration. (*Beit. Klin. Chir.* III.). Baumgarten and Crone studied other combinations of the two diseases about the mucous surface of the larynx, and in 1891 Zenker reported two quite classical cases of this character. In the first of them there was ulceration of the œsophagus, of epitheliomatous type. At the border of this ulcer it was easy to make out the presence of miliary tubercles in various stages of evolution, while within a little distance the mucous glands were in a stage of well-marked epitheliomatous proliferation. His second case concerned a tumor of the vocal cords, which proved to be typical epithelioma, while, along in close contact with it, were unmistakable foci of tubercular disease containing bacilli.

In pulmonary consumption, cancerous neoplasms have been repeatedly observed in connection with the tubercular lesions. Thus Friedlander has described a pavement epithelioma, with pearly bodies involving a lung cavity. (*Fortschrift. d. med.*, 1885, No. 10.) Menetrier thinks that the sclerosed tissue around such a cavity constitutes particularly favorable soil for the development of a primary epithelioma. Schawlbé has also reported a similar case of cancer, developed in the wall of a lung cavern. (*Virchow's Archiv.*

Vol. 149, p. 329.) The consideration of questions like these has led Ribbert to raise the question whether the disorganization of epithelial arrangement produced by the tubercular lesion may not be the exciting cause of the epithelial proliferation.

With Crone and Zenker, one must admit that the tuberculous process is at least capable of acting as an irritation which, like any other continued irritation, may provoke epithelioma, while at the same time it probably also lowers local tissue resistance. Warthin has reported somewhat recently a striking case, which is as follows (*American Journal Medical Science*, July, 1899): a woman of forty could not nurse her eleven-month-old baby, because on the right side was no milk, and because the left breast was painful and the nipple retracted. In this breast pain increased and a small tumor, hard and tender, appeared, which grew rapidly with axillary adenopathy. Exploratory puncture returned pus, containing tubercle bacilli. Subsequent operation revealed the presence of a number of tubercular nodules in various stages of degeneration, while at the same time there was a very distinct epitheliomatous formation in the connective tissue stroma, and around the nipple and the lymph spaces. The reporter considered that the tubercular process preceded the cancerous. He also reports a second case of a cancer of the breast associated with tuberculosis; in this case the tuberculosis appearing to be the second in the order of precedence.

Dufour (*Bull. de la Soc. Anat.*, February, 1898), has studied an endothelioma which he thought to be of arachnoidal origin, which lay in con-

tact with a focus of tuberculous ostitis at the lower end of the spinal column. The tumor did not appear to be infiltrated by tubercle, but inoculation gave a positive result, which could only be attributed to the presence of bacilli penetrating from the neighboring tubercular focus. Ribbert believes that the rarity of cancer transformation of visceral tubercular lesions is due to the rapid caseation which tubercular foci so placed undergo, the conditions being different from those obtaining in lupus of the skin, etc.

Lubarsch (*Virchow's Archiv*, III., p. 281) studied carefully the reports of autopsies in the Pathological Institute at Breslau for a period of twelve years. His analysis of 6,536 reports shows that 2,668 (*i. e.*, 41 per cent.) died of tuberculosis, and 569 (*i. e.*, nearly 9 per cent.) died of cancer. Of the 2,668 tubercular patients, 117 (4.10 per cent.), were cancerous. Of the 3,868 non-tubercular patients, 452 (11.7-10 per cent.) were cancerous. Of the 569 cancerous patients, to reverse the figures, 117 (20 per cent.) were tubercular, and of the 5,967 non-cancerous patients 2,251 (42.7-10 per cent.) were tuberculous. These figures will give a general idea of the relative frequency of the coexistence of these two diseases: that is, that in a general way, from 4 to 5 per cent. of tubercular patients suffer also from cancer, while about 20 per cent. of cancerous patients suffer from tuberculosis. The figures of Lubarsch have been fairly confirmed by results obtained elsewhere by Zenker, Cordua and Loeb.

The two diseases may be met with together, under the following conditions: (a) Independent co-existence where neither one seems to be in

any way related to the other; (b) Metastatic cancer developed upon old or recent tubercular lesion; Primary cancer actively appearing as a secondary infection; (d) Chronic tubercular lesion developing upon near a cancer; (e) Simultaneous development evincing almost a symbiosis.

The term cancer in this connection should be understood in its comprehensive significance implying more than mere epithelioma, though the latter is the most common of the manifestations in connection with tubercle. Iscovesco (*Bulletin de la Société Anat.*, 1888) reported to the Anatomical Society of Paris, in 1888, a case of sarcoma of the lung, simulating phthisis, where there were most distinct sarcomatous nodules in the pleura, with infiltration of the base of the lung, existing along with extensive tubercular cavities and a complete series of distinct disseminated tubercular granulations. Reich (*Abh. a. d. path. Inst. zu Göttingen*, 1893, p. 167) has reported a cerebral tumor composed of a combination of glioma and tuberculoma. Clement (*Virchow's Archiv.*, Bd. 139, 1899) has reported an endothelioma of the submaxillary region, complicated with tuberculosis. It occurred in a woman of fifty-two, and recurred after the first operation, so that a second attack was made upon it. Portions removed at this time gave the picture of endothelioma only, whereas the first specimen was distinctly tuberculous as well. Clement has also reported other cases; for instance, cancer of the lower jaw, with tuberculosis of the cervical lymphatics; another of cancer of the breast, with tuberculosis of the



FIG. 4. ACUTE MILIARY CARCINOSIS; LIVER. DR. WENDE.

axillary lymphatics; and another of cancer of the stomach, with ulceration of the mucosa, and, at the same time, distinct tuberculosis of the mesenteric lymphatics, and of the liver, without any trace of metastasis in these latter structures. Crawford (*Lancet*, 1892, p. 195) has described a scirrhous of the breast in which there was an abscess. In the tumor itself there were neither bacilli nor giant cells, but the axillary lymphatics were distinctly tubercular. I have myself recently treated a case of epithelioma of the palate, accompanied and followed by tuberculosis of the cervical lymphatics on both sides.

On the other hand, numerous observers have reported cases of tubercular lymph nodes transformed into malignant lymphoma. Askanazy (*Ziegler's Beitr. zur. Path. Anat.* III, p. 411), and Cordua (*Arbeit, a. d. Path. Inst. zu. Gottingen*, 1893) have both reported instances of this character where tumors have recurred after operation and have finally led to the death of the patient. I have myself seen within the past year and a half at least two cases where this combination seemed to me extremely evident, although in neither instance was I able to follow them up in such a way as to permit of a careful report which might positively establish the statement.

Ricker (*Archiv. fur. klinische Chirurgie*, Vol. 50, 1895.) has reported the following most suggestive instance: A boy of fifteen, who had for many years voluminous tumors upon the lateral region of the neck, was operated in 1890. Four years later another operation was undertaken because of a new collection of masses

in the same region, but was found to be so difficult that it was not fully completed. Section showed a distinct type of malignant lymphoma. The lad soon began to run down, and the tumors of the neck became adherent and ulcerated, other similar formations appeared, and the patient finally succumbed with paraplegia. At autopsy lesions were found in the neck, in the thorax, around the bronchi, in the lungs, in the adrenals, and in the vertebral canal. At this late point, the lesions seemed to amount to those of a generalized lymphomatosis. While this diagnosis could be made with a microscope without doubt, it was found at the same time that there was advanced tubercular disease in the neck, with caseation. Dietrich (*Beit. zur. klin. Chir.*, XI, 1896) and Fischer (*Archiv. fur. klin. Chir.*, 1897, Vol. 55) have also reported very characteristic cases in which the association of malignant lymphoma and tuberculosis was evident; thus Fischer reports two patients, of whom four died. Freyweiller (*Arch. fur. klin. Med.*, 1896) also has described recently an association between lymphomatous lesions and lymphatic tuberculosis. I have seen the same association of disease in a girl of ten.

Müller is quoted by Ricker to the following effect: A woman was operated on for tumor of the breast, considered sarcoma, which, however, was not subjected to a microscopic study. The operation was incomplete, and two years later there were found in the breast two distinct tumors, one the size of an apple, the other the size of a pigeon's egg. The patient seemed to be affected with a general sarcoma.

is. The former of these two tumors presented all the characteristics of a typical lympho-sarcoma. The latter contained distinct evidences of a seminated tubercle, and within its interior a distinct caseated mass, around which tubercular bacilli were easily found.

Tubercular infection complicating an already present tumor is probably the least known of the various processes here reported. There is no question, however, but that tubercle bacilli may penetrate into a cancerous growth and give rise there to tubercular foci, which latter may undergo the secondary changes common to such lesions in other parts of the body. Baumgarten and Crone (*Arbeit. a. d. Path. Inst. zu Tübingen* Bd. II.) report, for instance, the following: A man of forty-four, operated on for a small papilloma of the larynx, which when examined was found to be a small epithelioma. Some months later it recurred, tracheotomy was done, and the examination of portions of the tumor revealed the presence of distinct tubercular granulations. This was followed by extirpation of the larynx, which careful study showed a combination of cancer and tuberculosis, the same association being found in the lymphatics of the neck. Baumgarten, moreover, has observed about the same combination in a case of cancer of the rectum which was complicated by most evident tubercular granulations in the cancerous tissue. Friedländer (*Virchow's Archiv*. Vol. 60) has briefly reported the details of a case of cancer of the stomach, developed upon the base of a round ulcer, which base was surrounded with tuberculosis. Cordua (*Arbeit. a. d. Path. Inst. zu Göttingen*, 1893, p. 147)

studied a cancer of the oesophagus secondarily infected with bacilli, and came to the conclusion that the cancerous surface served as a point of least resistance and was attacked accordingly by the bacilli. Claude (*Cancer et Tuberculose*, Paris, 1900 p. 64) has reported the instance of a man of sixty-one entering hospital with an intense diarrhœa which had lasted for four months, and who at the same time had most marked cachexia. The autopsy showed extensive tubercular lesions of the large intestine, the lungs were also involved, while in the stomach a large cancerous tumor was found, surrounded by distinctly tubercular lesions. Evidently a portion of the tumor itself was breaking down with tubercular ulceration.

The following instance, illustrative of the close relation between injury and cancer growth, is reported by Steinhaus in a recent Polish journal (*Medycyna*, 1900 No. 47). A woman of forty applied a blister to her forehead on account of headache. As a result of this, there formed an ulcer which would not heal, and in spite of constant treatment, suppurated and discharged for five months. After that length of time the base of borders were excised and the defect filled by Thiersch grafts. After a few weeks, ulceration began at the point of operation and the Thiersch grafts were once more tried. Microscopic examination of the excised fragments showed the borders of the ulcer to have become cancerous. The case seems the more interesting as showing the peculiar effect of a chemical irritation applied for but a short time, since it is usually only long continued irritation which provokes cancerous growths.

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